RSF

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 10/645,250 | 08/20/2003 | Muktar A. Mahajan | 57953/1151 | 7913 |

7590 11/30/2005

Michael L. Goldman, Esq.
NIXON PEABODY LLP
Clinton Square
P.O. Box 31051
Rochester, NY 14603-1051

| EXAMINER | |
|---|---|
| AKHAVAN, RAMIN | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1636 | |

DATE MAILED: 11/30/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/645,250 | MAHAJAN ET AL. | |
| | Examiner | Art Unit | |
| | Ramin (Ray) Akhavan | 1636 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *20 August 2003*.

2a)☐ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-91* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-91* are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

Claims 1-91 are pending in this application. The claims encompass distinct inventions thus are subject to a restriction requirement.

### *Election/Restrictions*

Restriction to one of the following inventions is required under 35 U.S.C. 121 (each group designated with an Arabic numeral):

1. Claims 1-7, drawn to isolated human nucleic acids, expression vectors and cells comprising the same, wherein the invention is defined by sequences encoding NIF-1 (nucleic acids of SEQ ID NOs: 1, 3 and 4), classified in class 536, subclass 23.1.
2. Claims 1-7, drawn to isolated human nucleic acids, expression vectors and cells comprising the same, wherein the invention is defined sequences encoding NIF-2 (nucleic acids of SEQ ID NOs: 5 and 6), classified in class 536, subclass 23.1
3. Claims 8-14, drawn to antisense molecules, wherein the invention is defined by sequences encoding NIF-1 (nucleic acids of SEQ ID NOs: 1, 3 and 4), classified in class 536, subclass 24.5.
4. Claims 8-14, drawn to antisense molecules, wherein the invention is defined sequences encoding NIF-2 (nucleic acids of SEQ ID NOs: 5 and 6), classified in class 536, subclass 24.5.
5. Claims 15-17, drawn to proteins having the amino acid sequence of SEQ ID NO: 3, classified in class 530, subclass 350.

6. Claims 15-17, drawn to proteins having the amino acid sequence of SEQ ID NO: 6, classified in class 530, subclass 350.
7. Claims 18-22, drawn to antibodies raised against a protein having the sequence of SEQ ID NO: 3, classified in class 424, subclass 130.1.
8. Claims 18-22, drawn to antibodies raised against a protein having the sequence of SEQ ID NO: 6, classified in class 424, subclass 130.1.
9. Claims 89-91, drawn to an isolated rat nucleic acids, classified in class 536, subclass 23.1.
10. Claims 23-25, drawn to a method of *regulating cell proliferation* by transfecting said cell with *nucleic acids encoding a particular NIF protein*, classified in class 435, subclass 455.
11. Claims 26-28, drawn to a method of *regulating cell differentiation* by transfecting said cell with *nucleic acids encoding a particular NIF protein*, classified in class 435, subclass 455.
12. Claims 29-31, drawn to a method of regulating *cell development* by transfecting said cell with *nucleic acids encoding a particular NIF protein*, classified in class 435, subclass 455.
13. Claims 32-34, drawn to a method of *modulating transcriptional co-activator complex activity* in a cell by transfecting said cell with *nucleic acids encoding a particular NIF protein*, classified in class 435, subclass 455.

14. Claims 35-37, drawn to a method of modulating transcriptional co-activator complex activity in a cell by transfecting said cell with an *antisense molecule against a particular NIF protein*, classified in class 435, subclass 455.
15. Claims 38-40, drawn to a method of modulating transcriptional co-activator complex activity in a cell by *contacting said cell with a particular NIF protein*, classified in class 424, subclass 85.1.
16. Claims 41-43, drawn to a method of modulating transcriptional co-activator complex activity in a cell by *contacting said cell with an antibody raised against particular NIF protein*, classified in class 424, subclass 85.1.
17. Claims 44-47, drawn to a method of *regulating hormone receptor activity* in a cell by *contacting said cell with a particular NIF protein*, classified in class 424, subclass 85.1.
18. Claims 48-51, drawn to a method of *regulating hormone receptor activity* in a cell by *contacting said cell with an antibody raised against a particular NIF protein*, classified in class 424, subclass 85.1.
19. Claims 52-55, drawn to a method of *regulating hormone receptor activity* in a cell by *transfecting said cell with nucleic acids encoding a particular NIF protein*, classified in class 435, subclass 455.
20. Claims 56-59, drawn to a method of *regulating hormone receptor activity* in a cell by *transfecting said cell with antisense molecules targeted against nucleic acids encoding a particular NIF protein*, classified in class 435, subclass 455.

21. Claims 60-63, drawn to a method of *modulating activity of a transcription factor* in a cell by *transfecting said cell with nucleic acids encoding a particular NIF protein*, classified in class 435, subclass 455.

22. Claims 64-67, drawn to a method of *modulating activity of a transcription factor* in a cell by transfecting said cell with *antisense molecules targeted against a particular NIF protein*, classified in class 435, subclass 455.

23. Claims 68-70, drawn to a method of *modulating endocrine function* in a subject by *treating said subject with nucleic acids encoding a particular NIF protein*, classified in class 514, subclass 44.

24. Claims 71-73, drawn to a method of *modulating endocrine function* in a subject by *treating said subject with antisense molecules targeted against a particular NIF protein*, classified in class 514, subclass 44.

25. Claims 74-76, drawn to a method of *modulating endocrine function* in a subject by *treating said subject with a protein encoding a particular NIF protein*, classified in class 514, subclass 2.

26. Claims 77-79, drawn to a method of *modulating endocrine function* in a subject by *treating said subject with antibodies raised against a particular NIF protein*, classified in class 424, subclass 130.1.

27. Claims 80-82 or 86-88, drawn to a method of *treating diabetes or insulin resistance* by treating a subject with *a protein encoding a particular NIF protein*, classified in class 514, subclass 2.

28. Claims 83-85, drawn to a method of *treating diabetes* by treating a subject with *an antibody raised against a particular NIF protein*, classified in class 424, subclass 130.1.

At the outset it must be noted that in order to set forth a more concise, organized and more easily discernible restriction requirement, certain groups outlined above comprise more than one invention. More particularly, the groups outlining various methods, which encompass biologically and patentably distinct products have been set forth as designated by a single Arabic numeral. More precisely, Groups 10-28 encompass utilization of distinct nucleic acid molecules as defined by sequences encoding *NIF-1* or *NIF-2* (i.e., SEQ ID NOs: 1, 3, 4 and 5, 6, respectively), distinct proteins encoding *NIF-1* or *NIF-2* (i.e., SEQ ID NOs: 3 and 6, respectively), distinct antisense molecules targeting nucleic acid molecules of *NIF-1* or *NIF-2* (i.e., SEQ ID NOs: 1, 3, 4 and 5, 6, respectively) and antibodies raised against *NIF-1* or *NIF-2* proteins (i.e., SEQ ID NOs: 3 and 6, respectively). As such if any of Groups 10-28 is elected for examination, notwithstanding traversal of the restriction requirement, Applicant must in effect also elect either NIF-1 or NIF-2.

In view of the foregoing, there are actually 47 distinct inventions (i.e., one invention each in Groups 1-9 and two inventions each in Groups 10-28)[1]. In general, the inventions are directed to patentably distinct products and patentably distinct processes. Before addressing how the different inventions are patentably distinct, it should be noted that certain claims are subject to a Species Election as discussed below (*infra*, Species Election). Furthermore, certain claims are linking claims insofar as said claims link patentably distinct inventions.

[1] Applicant is welcome to contact the Office if clarification is needed.

In particular the claims are linking claims that link nucleic acids, proteins, antisense molecules and antibodies directed against patentably distinct NIF-1 and NIF-2. The restriction requirement for the linked inventions is subject to the nonallowance of the linking claims, claims 1, 2 (nucleic acids), 15 (proteins) and 18 (antibodies). Upon the allowance of the linking claims, the restriction requirement as to the linked inventions shall be withdrawn and any claims depending from or otherwise including all the limitations of the allowable linking claims will be entitled to examination in the instant application. For example, if Applicant elects a method that is the same but for said nucleic acids, proteins or antibodies being directed to NIF-1 or NIF-2, if the method is deemed allowable for NIF-1 then the restriction requirement as to NIF-2 shall be withdrawn.

Applicant is advised that if any such claims depending from or including all the limitations of the allowable linking claims is/are presented in a continuation or divisional application, the claims of the continuation or divisional application may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application. Where a restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. *In re Ziegler*, 44 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

The nucleic acids of Group 1 and 2 are comprised of distinct structures (i.e., sequences) thus are patentably distinguishable. In other words, inventions in Group 1 and 2 are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are defined by distinct

nucleotide sequences that encode NIF-1 and an alternatively spliced product – NIF2 (i.e., SEQ ID NO: 1 and SEQ ID NO: 5, respectively). Neither the claims nor the specification are directed to said NIF-1 and NIF-2 nucleic acids as being concomitantly utilized in the various methods disclosed. Further, since the sequences have distinct structures, each encodes a polypeptide by a different mode of operation. Moreover, a search of the varied and ever increasing in number sequence databases for one sequence would not yield the other. Thus, searching for the distinct nucleic acid sequences would be overly burdensome.

It follows that the groups directed to antisense molecules (Groups 3 and 4), proteins (Groups 5 and 6), and antibodies (Groups 7 and 8) are similarly distinct based on encoding distinct amino acid sequences, comprising distinct proteins and distinct antibodies. In other words, in each case the structures are different thus patentably distinguishable based on *NIF-1* versus *NIF-2*. Further, searching the non-patent literature for a particular sequence, whether of an antisense molecule, protein, or searching for a particular antibody would not necessarily yield the other.

In addition, Group 9 is directed to an altogether different sequence (i.e., isolated rat nucleic acid of SEQ ID NO: 7). Clearly the sequences are of distinct sequences as well as of varying size (e.g., SEQ ID NO: 7 is 2778 nucleotides versus, 4439 and 2662 nucleotides for SEQ ID NO: 1 and 5, respectively).

As between nucleic acid molecules versus antisense molecules (Groups 1-2 versus Groups 3-4), the inventions are unrelated because in each case a specific structure (i.e., sequence) corresponds to a particular functionality (e.g., encoding a protein(s) versus antisense molecules which are interpreted as molecules inhibiting expression of proteins, such as through

inhibiting transcription or translation). Therefore, while both class of inventions are based on nucleic acid molecules, in each case the structures and functions are both biologically and patentably distinguishable. Furthermore, the sequence requirements for antisense function are not as stringent as for encoding a functional protein (e.g., complementarities between target and antisense molecule sequences is not as stringently required as with sequences encoding a protein).

As amongst the various products of Groups 1-9, each set[2] of groups directed to nucleic acids, proteins and antibodies is defined a unique structure that corresponds to a unique function. Clearly, nucleic acids are distinct structures as compared to proteins or antibodies. Similarly, proteins and antibodies are distinct from each other, as each is comprised of biologically and patentably distinct structures that correspond to a particular function (e.g., encoding a protein function versus binding a particular epitope with some specificity). Furthermore, a search for one set would not necessarily be co-extensive with another. For example, a particular non-patent literature publication may disclose a protein without any reference to an antisense molecule, or an antibody molecule. In sum, the products of Groups 1-9 are patentably distinguishable.

The various methods of Groups 10-28 are directed to biologically and patentably distinct outcomes and entail utilizing distinct modes of operation, involve different components/element or steps. As noted above, on one level, where a particular group is directed to a method that involves linked inventions, the group actually comprises two distinct inventions (i.e., based on NIF-1 and NIF-2).

---

[2] The term "set" corresponds to inventions that are similar insofar as being directed to a product class, e.g., proteins.

On a second level, where the method (i.e., group) is directed to the same outcome but utilizes materially different components/elements/steps, the methods are patentably distinct (i.e., Groups 13-16: *modulating transcriptional co-activator complex activity in a cell*; Groups 17-20: *regulating hormone receptor activity in a cell*; Groups 21-22: *modulating activity of a transcription factor*; Groups 23-26: *modulating endocrine function in a subject*; and Groups 27-28: *treating diabetes in a subject*). In particular, each group is distinguishable from the next, where the groups are directed to transfecting cells with nuclei acids encoding a particular NIF protein, contacting cells with said protein, contacting cells with antisense molecules targeting said protein, or contacting cells with an antibody raised against said protein. Put another way, the modes of operation for each method is distinguishable based on the component or element utilized (e.g., antisense versus antibody). As such, searching for one method, involving a distinct step utilizing a patentably distinguishable product would not necessarily yield any other method involving a different step utilizing a second distinct product.

On a third level certain methods are directed to a different outcome but utilize the same modes of operation (i.e., Groups 10-13, 19, 21: *tansfecting cells with nucleic acids of Group 1-2*; Groups 14, 20, 22: *transfecting cells with antisense molecules*; Groups 16 and 17: *contacting cells with a protein*; Groups 16 and 18: *contacting cells with an antibody*). For example, each of Groups 10-12 is directed to a different outcome but each effects the recited outcome by transfecting cells with nucleic acids of Groups 1 and 2. Where the groups (i.e., methods) are directed to different outcomes but utilize the same exact steps, the methods are deemed patentably distinguishable insofar as conditions necessary to effect a certain claimed limitation would be distinct. For example, in Group 10 (claims 23-25), conditions must be effective to

regulate cellular proliferation, or in Group 11, conditions must be effective to regulate cell differentiation.

In each of the groups, where a distinct outcome is recited, the cellular pathways and components involved are patentably distinct thus searching for one outcome with the same step would not necessarily yield another potentially novel outcome. By analogy, one can consider a method of alleviating a headache by administering to aspirin to a subject. Now one can consider a potentially novel method, where the same step of administering aspirin to a subject is aimed to prevent a heart attack. Thus, the same step is utilized in a method that is patentably distinguishable and certainly would involve independent search. In sum, as the foregoing discussion highlights, the claims encompass patentably distinct products and patentably distinct processes.

Inventions in Groups 1-8 and Groups 10-28 are related as products and processes of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case as is evidenced by the various methods in the disclosure, the same products can be utilized in materially distinct processes.

However, it should be noted that where the examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. **Process claims that depend from or otherwise include all the limitations of the**

**patentable product** will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai, In re Brouwer* and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.** Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the examiner withdraws the restriction requirement before the patent issues. See MPEP § 804.01.

***Species Election***

This application contains claims directed to the following patentably distinct species of the claimed invention: the recited hormone receptors (i.e., claims 45, 49, 53, 57) and the recited transcription factors (i.e., claims 61, 65). Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no

generic claim is finally held to be allowable. Currently, claims 44, 48, 52, 56, 60 and 64 are generic.

Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a). Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art, and would require a separate search, restriction for examination purposes as indicated is proper.

### *Conclusion*

The claims encompass multiple distinct inventions thus are subject to a restriction requirement.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ramin (Ray) Akhavan whose telephone number is 571-272-0766. The examiner can normally be reached on Monday-Friday from 8:30-5:30. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, Ph.D. can be reached on 571-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Respectfully submitted,

Ray Akhavan/AU 1636

DANIEL M. SULLIVAN
PATENT EXAMINER